

## IN THE SPECIFICATION

Please insert the following paragraph on page 1, line 2, after the title:

--This is a continuation-in-part of allowed U.S. application Serial No. 09/915,169, filed on July 25, 2001, which is a divisional application of U.S. application Serial No. 09/224,014, filed on December 28, 1998, now U.S. Patent No. 6,312,682, which is a continuing application of PCT/GB97/02857, filed October 17, 1997 and claiming priority to Great Britain Patent application Nos. 9621680.9, filed on October 17, 1996, and 9624457.9, filed on November 25, 1996. This application makes reference to U.S. application Serial No. 10/408,456, filed on April 7, 2003.

All of the foregoing applications, as well as all documents cited in the foregoing applications ("application documents") and all documents cited or referenced in the application documents are incorporated herein by reference. Also, all documents cited in this application ("herein-cited documents") and all documents cited or referenced in herein-cited documents are incorporated herein by reference. In addition, any manufacturer 's instructions or catalogues for any products cited or mentioned in each of the application documents or herein-cited documents are incorporated by reference. Documents incorporated by reference into this text or any teachings therein can be used in the practice of this invention. Documents incorporated by reference into this text are not admitted to be prior art.--

Please replace the paragraphs beginning on page 11, line 9, with the following rewritten paragraphs:

-- The construction of pTIN406, pTIN408 and pTIN414 has been described (Cannon *et al.*, 1996). The 5' LTR of pH3Z and pH4Z contain a CMV promoter at the U3 position and the HIV R and U5 regions. HIVdge was made from HIVgpt (Page *et al.*, 1990) by blunt-ending the Cla I site (829) to create a frameshift mutation. HIVdge was cut with Bgl II and Pst I (473-1414) and inserted into pTIN406. pTIN406 has an LTR structure of CMV, R (HIV) and U5 (MLV). This created a hybrid LTR containing CMV, and R, U5 from HIV called pBS5'. To provide the plasmid with *rev* and RRE the Eco RI/Xho I fragment (5743-8897) was cut from HIVdge1.2 which is a HIVdge derivative containing a deletion from Nde I to Bgl II (6403-7621) and was inserted~~inserting~~ into pBS5' to create pBS5'R. The 3' LTR was provided by inserting the Not I/Xho I fragment of pBS3' into pBS5'R creating pH2. pBS3' was created by a three way ligation of the Xho I/Hind III fragment of pWI3, the Hind III/Kpn I fragment of pTIN408 into Bluescript

KS+ (Xho I/KpnI). A CMV promoter was inserted into the unique Xho I site of pH2 from pSPCMV (Sal I/Xho I) making pH2CMV. pSPCMV was created by inserting pLNCX (Accession number: M28246) (Pst I/Hind III) into pSP72 (Promega). The  $\beta$ -galactosidase gene was inserted from PTIN414 into pSP72 (Xho I/Sph I) to make pSP $\beta$ lacZ. A Xho I/Sal I digest of pSP $\beta$ lacZ gave the  $\beta$ -galactosidase coding region which was inserted into pH2-CMV to give pH3Z. pH4Z was constructed to create *tat*-deficient vector. The first 50 bp of the *tat*-coding region was removed by replacing EcoRI (5743)I-SpeI fragment in pH3 with EcoRI (5881)-SpeII PCR product amplified using PCR primers DELT5 (5'-CGTGAATCGCCTAAAATGCTTGTACCA-3') (SEQ ID NO:1) and DELT3 (5'-GAACTAATGACCCCGTAATTG-3') (SEQ ID NO:2) to create pH4. The Nsi I/Spe I fragment from pH4 was inserted into pH3Z to generate pH4Z.

A *vpr* expression plasmid was constructed by PCR amplification of the *vpr* coding region from pNL4.3 (Accession number: U26942) using the following primers: 5' primer GCGAATTCTGGATCCACCATGGAACAAGCCCCAGAAGAC (5563-5583) (SEQ ID NO:3) and 3' primer GCGAATTCTGGATCCTCTAGGATCTACTGGCTCCATT (5834-5853) (SEQ ID NO:4). This amplicon was cloned into pLIGATOR (R&D Systems). The expression plasmid pCl-*vpr* was made by inserting the Mlu I and Xho I fragment containing the *vpr* coding region into pCl-Neo (Promega).--